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EXPERIMENTAL STREPTOCOCCUS ARTHRITIS IN RELATION TO THE ETIOLOGY OF ACUTE ARTICULAR RHEUMATISM.*

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THE following theories as to the etiology of acute articular rheumatism are held by those who believe in its bacterial origin:

1. That it is due to a specific micro-organism, as yet undiscovered.
2. That it is due to various pyogenetic cocci, mainly the ordinary streptococci; that it is a mild form of pyemia.
3. That it is due to a specific streptococcus or diplococcus.
4. That it is due to a specific bacillus—Bacillus of Achalme.

The evidence adduced by those holding the last view is not at all convincing. At present the second and third views have most supporters, and it is mainly these that we propose to consider.

The view that acute articular rheumatism is caused by streptococci or diplococci is based, first, on the isolation by various observers from the blood, joints, urine, or inflammatory exudates in certain cases, clinically resembling acute articular rheumatism, of streptococci or diplococci; and, second, by the production of arthritis and endocarditis in rabbits by the introduction of pure cultures of these organisms into the circulation. Furthermore, for a long time a close relationship between angina and rheumatic fever has been recognized, and Meyer has cultivated from the throats of rheumatic patients suffering from angina streptococci which when introduced into rabbits also produced arthritis and endocarditis.

Without reviewing in detail the results of the various observers who have cultivated cocci from cases of rheumatic fever, we may say that all investigators have not had similar fortunate results.

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* Received for publication October 5, 1904.

With a fairly generally distributed organism like the streptococcus, the possibility of contamination must always be borne in mind, and the possibility, in the more severe cases at least, that the streptococcus infection is a terminal or secondary one, must be considered. Streptococci are so frequently found in the throat, especially in all forms of angina, that the importance of their presence in rheumatic angina must rest entirely with the demonstration of specific characteristics. So also the difficulty in differentiating acute rheumatism from certain cases of septic arthritis and acute forms of arthritis deformans adds to the chances for error.

During the past three years, in practically all cases of acute articular rheumatism treated in this hospital routine cultures have been made from the blood, and from the joints whenever any effusion was present in the latter. So far all our cultures from cases of acute articular rheumatism have been negative. Similar results have been obtained by Philip,[1] who made cultures twenty-one times from the blood and six times from the joints in twenty-four cases of acute articular rheumatism, and also made cultures twice from the blood and twice from the joints in four cases of chronic rheumatism (arthritis deformans). The cultures were made in a great variety of both solid and liquid media, and were cultivated both aërobically and anaërobically. Inoculations directly from patients were also made into guinea pigs, rabbits, dogs, monkeys, and calves. But from none of these cases could any bacteria be cultivated.

The view that the cocci hitherto cultivated from rheumatic cases are specific, *i. e.*, differ inherently from the ordinary Streptococcus pyogenes, is based mainly on the supposedly characteristic effects when introduced into rabbits, and to a less extent on certain cultural and morphological peculiarities. The main characteristic pathogenic effects claimed have been the development of a multiple arthritis, and in certain cases endo- and pericarditis. Meyer[2] laid stress on the mild character of the arthritis and the absence of bacteria in the affected joints, though other observers, making the same claim of specificity for this streptococcus, repeatedly cultivated the organisms from the inflamed joints. However, "long ago Loeffler, with a streptococcus isolated from a case of scarlet fever angina, repeatedly produced joint inflammation, indeed so often that he definitely spoke of a 'streptococcus articulorum.' It is further quite well known that Buday produced polyarthritis in animals with streptococci isolated from a septic joint infection" (quoted by Singer[3]). Also Menzer, by the injection of a streptococcus isolated from a breast abscess, and of a second one isolated from a case with septic endocarditis, produced effects in rabbits similar to those which had been reported by Meyer with streptococci from rheumatic angina, and by Westphal, Wassermann, and Malkoff[4] with streptococci from a case of chorea, and by Menzer and others from rheumatic fever cases. The evidence up to 1902 in regard to the bacterial etiology of rheumatic fever has been all collected and reviewed by Menzer,[5] and I have, therefore, not detailed the previous observations. Menzer concluded:

> The cause of acute articular rheumatism is not a specific bacterium, but the ordinary parasites of the mouth, which under certain conditions have become pathogenic. Almost exclusively are streptococci the organisms concerned. These streptococci are by far the most common cause of the different forms of angina, and also of the so-called angina rheumatica.

Since the publication of Menzer's monograph, however, several English observers* have continued to report the isolation and study of a diplococcus or streptococcus from the blood, joints, urine, or inflammatory exudates of certain cases clinically resembling acute rheumatic fever. This organism they regard as a specific micro-organism, and consider as a cause (some of them as *the* cause) of rheumatic fever, and for it Walker has proposed the name Micrococcus rheumaticus. Poynton and Paine have not claimed the discovery of this organism, but in their earlier papers have endeavored to show its identity with the organisms described previously by Triboulet, Dana, and Westphal, Wassermann and Malkoff. As the present paper proposes to deal with the claim as to the specificity of the organisms described, it will not be necessary here to give the details as to the manner of isolation and source of the organisms studied.

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*Poynton and Paine, Ainley Walker, Beaton and Walker, Shaw, Beattie. (See list of references at the end of this paper.)

The claims of the various writers as to specificity of the organisms isolated are based on morphological, cultural, and pathogenic peculiarities of the organism isolated. In the various papers published, reports, usually quite meager, of the morphological and cultural characteristics are given. But in none of them have I been able to find any definite characters given which will serve definitely to identify this organism from the ordinary Streptococcus pyogenes. In the first reports it was spoken of as a diplococcus, then as a diplococcus frequently growing in chains, and in some of the papers very long chains are described.

To summarize briefly the results obtained in the efforts to separate this coccus on morphological or cultural grounds; we cannot do better than quote certain conclusions from the papers of Beaton and Walker and of Shaw, whose papers (except that of Beattie, which adds nothing to this aspect of the subject) have appeared last and deal more extensively with the cultural and morphological characteristics than the others have done. Walker says:

> This organism has been classed by Paine and Poynton as a diplococcus; by the German workers it is usually called a streptococcus. So far as our own observations go, the pairing of the cocci is usually very marked in recent cultures, and more especially in the original cultivations, and in body fluids or on agar-agar; and chains may be quite infrequent in the films. Under cultivation the arrangement in chains becomes more marked, and cultures grown in milk or in a highly alkaline bouillon frequently present long chains, which in some cases may extend across one or more fields of the microscope with a one-twelfth oil immersion objective. When growing in the tissues— as, for example, in endocarditic vegetations in the human subject—the majority of the cocci are seen to be in pairs, but sections not infrequently show chains of half a dozen individuals or more.
>
> Whether the micrococcus be spoken of as a diplococcus or a streptococcus does not appear to be of any great importance, and might be regarded merely as a matter of words.
>
> But we think that the persistent application of the former term to an organism which is at present indistinguishable on culture media from an ordinary streptococcus, and which in cultures often shows a marked tendency to grow out into chains, has probably tended to delay considerably its general recognition by bacteriologists: for we have no hesitation in saying that *without animal experiments it would almost certainly be diagnosed as an ordinary streptococcus by anyone* [italics ours] to whom cultures and stained preparations were submitted without comment.
>
> Culturally this organism resembles a streptococcus, but that it is specifically different from the ordinary streptococci is rendered probable by our results on the application of the test of Marmorek.

Since, however, the value of this test for determining specificity has had so much doubt thrown upon it by the work of Meyer,[11] and Aronson,[12] and others, and especially since Walker's observations were so few and reported with such slight detail, this evidence at present, at least, cannot be considered very valuable.

Shaw's results are especially important in this connection, as he worked with organisms obtained from several observers. He describes the organism as a "streptococcus, and, though usually smaller than the Streptococcus pyogenes commonly met with, *it might easily be mistaken for it* [italics ours]. It grows well on the ordinary nutrient media." The only characteristic given which might serve to separate it from Streptococcus pyogenes is the following: When grown on blood agar "the blood agar undergoes a change in color. The bright red color is replaced by a dull brown or rusty appearance, or even a greenish-brown tint." He says: "In the case of several other varieties of micrococci investigated, this alteration in color does not occur, *e. g.*, with the *Streptococcus pyogenes* and the *Streptococcus septicaemiae*" (?).

Reference to a publication of Schottmüller's,[13] however, shows that a similar reaction has been described as occurring with a large number of streptococci obtained from widely differing sources, none of which were rheumatic fever cases. These races have been grouped by that writer into a separate variety, to which he gives the name *Streptococcus mitior seu viridans*, in contra-distinction to the variety *Streptococcus longus pathog. seu erysipelatos*, by which only hemolysis of the blood medium is produced, but no discoloration. He calls special attention to the fact that in the cases where the former variety occurred the infection was milder than that associated with the latter variety.

It is further stated by Shaw that

> the characteristics described above apply, in the first place, to the organism isolated by Wassermann and Westphal, but they apply, without modification, as far as morphology and cultural characteristics go, to the micrococcus kindly sent me by Dr. E. W. A. Walker from Guy's Hospital, and to that sent by Dr. F. J. Poynton from the Hospital for Sick Children, Great Ormond Street.

From all this it is evident that at present the claims for specificity of this organism must rest on the results obtained by inoculation into animals.

Practically all of the observers who have been mentioned as describing a coccus associated with rheumatic fever, have been able, by the inoculation into rabbits of quite large amounts of this streptococcus, to induce multiple arthritis of variable grades of intensity, in some cases endocarditis and pericarditis, and in a few experiments a condition said by the writers to resemble chorea. It would lead us too far to attempt a detailed description and report of the experiments of these observers whose papers are all easily accessible.

WRITER'S OWN EXPERIMENTS.

While making a series of cultures from cases of acute rheumatic fever and endocarditis, a streptococcus was cultivated from the blood of the patient whose history is given below in abstract.

STREPTOCOCCUS FROM CASE "RAND."

BARBER, COLORED, AGED FIFTY. ADMITTED NOVEMBER 12, 1903.

The patient said he had always been quite well up to five or six years before admission, when he began to have "heart trouble." For a year or more he had been troubled with "rheumatic pains in his joints," though no definite history of acute rheumatic fever could be obtained.

Following a spree four weeks before admission, the patient noticed swelling of both legs, right hand, and arm, and he complained of headache and pains in his joints. He soon became slightly irrational. This lasted a few days, and then he became suddenly unconscious, and it was found there was complete right-sided hemiplegia. The right arm was constantly in motion with spasmodic movements. The mental condition began to clear up on the third day, and there was gradual improvement in the muscular power. On November 10 there came another sudden attack of unconciousness, and again complete loss of power on right side.

On admission he apparently understood what was said to him, but could not articulate distinctly. There was almost complete right-sided flaccid hemiplegia. The area of cardiac dulness was moderately increased. The heart action was very irregular, and there were signs of aortic and mitral insufficiency. There was no edema of extremities, and no definite signs of arthritis could be made out. Temperature, 101°5; pulse 100.

The patient remained in about the same condition, the temperature being continually elevated, ranging between 100° and 103°, until November 17, when a blood culture was taken and a streptococcus isolated, the number of colonies averaging about 6 to 1 c.c. of blood. The patient's condition gradually grew worse, and death occurred on December 7. At no time was any arthritis made out. The clinical diagnosis was acute endocarditis, cerebral embolism, septicemia. Cultures from the blood were made, as above stated, on November 17, and again on November 20, on the latter date about 30 colonies developing from each cubic centimeter of blood. On November 24 cultures were again made from the blood, about thirty-five colonies to each cubic centimeter developing, and on November 30 blood cultures again showed streptococci in about the same number. On December 6 blood cultures were again made, with a like result.

Autopsy showed as the principal lesions acute and subacute vegetative mitral and aortic endocarditis, cardiac hypertrophy and dilatation, chronic passive congestion of the internal viscera, multiple infarction of spleen and kidneys, thrombosis of left middle cerebral artery, with extensive softening of the internal capsule.

Although this organism grew well on ordinary media, and culturally no difference from the common Streptococcus pyogenes could be made out, it was thought, owing to the presence of endocarditis and history of a previous attack of rheumatism, that possibly the organism was identical with the so-called "Micrococcus rheumaticus;" so a series of inoculation experiments was undertaken. The study of this organism formed the beginning of the present series of observations.

As the organism grew rather better on glycerin agar than on plain agar, and as most of the inoculation experiments reported by the English observers had been made with emulsions made of the growth on dry media, either blood agar or glycerin agar, it was thought best to continue the use of this medium and method for the inoculation material. Slant 6 per cent. glycerin agar tubes were used, and the inoculating material was thoroughly smeared over the surface with a platinum needle. After twenty-four hours' growth about 1 c.c. of bouillon was poured over each tube, and the growth scraped off with a platinum needle and thoroughly mixed with the bouillon. After the desired number of tubes of suspension had been so prepared, they were poured together into a sterile dish, and the fluid drawn into a glass syringe and in all cases inoculated into the ear vein, being careful that it all entered the vein and did not spread subcutaneously. In this way ear abscesses were avoided almost entirely.

INOCULATION EXPERIMENTS.

Rabbit I.—Rabbit apparently healthy. Temperature, 99°.6.

XI-28: Inoculation into the ear vein of an emulsion made from growth on four glycerin agar tubes (twenty-four hours' growth).

XI-29: Rabbit apparently well.

XI-30: Lame in left front leg: will not put left foot to ground; hops about on three legs; the left elbow is swollen and sensitive. Temperature, 101°.8.

XII-1: Some improvement in the left fore leg, but there appeared to be some soreness in the left hind leg. Temperature, 102°.4.

XII-2: Left hind leg still seems tender. Temperature, 100°.8.

XII-3: Condition better, no lameness. Temperature, 99°.6. Reinoculated; emulsion made from growth on five glycerin agar tubes (twenty-four hours' growth). There was no lameness or swelling of the joints following this inoculation; temperature ranged between 99°.4 and 99°.8, and animal did not appear sick until XII-9, when the temperature was 101°, and the rabbit was quite lame in the left hind leg. The lameness persisted until XII-13, when death occurred. The autopsy showed slight reddening of the inner surface of the capsule of the left hip joint and a small amount of slightly turbid, thick, tenacious, exudate in the joint. There was no roughening of the cartilage. A similar condition was found in the left elbow. All the other joints appeared normal. There were no microscopic lesions in any of the viscera. Smears were made of the exudate in the left hip and elbow. These were stained with an aqueous solution of methylene blue. From both joints the cellular constituents of the exudate were found to be mainly polymorphonuclear cells, with a few large mononuclear cells. A few biscuit-shaped diplococci were found in smears from each joint.

The upper part of the left femur, with as much of the capsule of the joint as possible attached, was hardened in alcohol and decalcified in a nitric acid solution. Longitudinal sections through this piece show a mild inflammation of the superficial layers of the inner surface of the capsule, especially marked at the edge of the cartilage and just outside this line. The surface is covered by a small amount of exudate containing mostly polymorphonuclear leucocytes and a few red blood corpuscles. The cartilage covering the head of the bone is quite smooth and unaffected.

Unfortunately the records from cultures of this rabbit have been lost.

Rabbit II.—Rabbit apparently healthy. Temperature, 99°4.

XII-9: Inoculation into the ear vein of an emulsion made from the growth on six glycerin agar tubes (twenty-four hours' growth).

The rabbit appeared to be stiff in its movements several days after the inoculation, though at no time could any definite lameness or swelling of the joints be made out. The temperature ranged between 100° and 102° from XII-12 to XII-20, on which day the animal died.

At autopsy all of the joints were carefully examined, but no macroscopical lesions were found in any except the left shoulder, where the inner surface of the capsule showed considerable redness, and there was a small amount of tenacious, sticky, muco-purulent exudate. No erosion of the cartilage was seen. The internal organs appeared normal. Cultures made from the heart's blood, liver, kidney, spleen, gall bladder, right shoulder, left elbow, and right knee showed no growth. The culture from the left shoulder showed a growth of streptococci which were identified as identical with those inoculated.

Smears made from the exudate in the left shoulder joint showed many polymorphonuclear leucocytes and some large mononuclear cells. A moderate number of diplococci were seen. These were usually oval with the long axis transverse to the direction of the pair and the adjacent surfaces slightly flattened. No chains were found.

The left shoulder, with portion of the humerus and scapula, was hardened, decalcified, sectioned, and stained. The sections show a considerable infiltration of the capsule, and swelling and infiltration of the villous projections. There is no erosion or roughening of the cartilage. The infiltration is mainly with polymorphonuclear cells.

Rabbit III.—This rabbit had two inoculations, the first on XII-17 of an emulsion from six glycerin agar tubes (twenty-four hours' growth), and again on XII-29 of an emulsion from the growth on six glycerin agar tubes, the organism used for the latter growth being that obtained from the joint of Rabbit II. After the first inoculation no lameness was made out, but after the second inoculation, on XII-31, there were definite tenderness and lameness in the right fore leg and in the left hind leg. No swelling of the joints could be detected.

The autopsy showed a mild involvement of the right shoulder, left hip, and right hip, similar to that seen in Rabbits I and II.

Cultures made from the heart's blood, left knee, left hip, left elbow, right hip, right knee, and right elbow were all sterile. On the plate made from the right shoulder there developed about twenty colonies, all of which were alike, and which were proved to be streptococci like those inoculated.

Although there was no growth from the right hip, smears of the exudate made from this joint showed a few diplococci. No diplococci, however could be made out in smears from the left hip, though the exudate was quite purulent, more so than that in the right hip.

Sections were made through both hips and show quite marked infiltration of the villi and capsule near its junction with the cartilage with small round cells and polymorphonuclear leucocytes. There is considerable congestion apparent about the joint, and the exudate into the joint shows many pus cells, as well as mononuclear cells. The left hip shows more marked changes than the right.

Rabbit IV.—XII-29: Inoculation into the ear vein of an emulsion made from the growth on six glycerin agar tubes (twenty-four hours' growth). The organism in this case was that obtained from the left shoulder of Rabbit II.

On the third day following the inoculation the rabbit began to appear sick, would not move unless urged, and all its joints appeared painful; the animal would not use the left hind leg. This lameness and stiffness continued, at times one extremity appearing more lame, and again another. The animal lost rapidly in weight. The lameness, however, grew less, and on I-11 it was inoculated intravenously with an emulsion made from the growth on six glycerin agar tubes (twenty-four hours' growth) of organism from Rabbit II. On I-14 the lameness and stiffness in joints again began, especially marked in the left hind leg. This again disappeared by I-19. On this day a similar reinoculation was made as on previous occasions. On this occasion the lameness and stiffness were not evident until a week after the inoculation. Again, while the lameness was quite general, it was most marked in the left knee. This lameness lasted three days. Following this, the rabbit was inoculated on I-29, II-16, III-1, III-29, and IV-7, on each occasion lameness and stiffness of the joints appearing four to seven days after the inoculation. As, however, the lameness and joint involvement became less with the later inoculation, it was thought well to try the effect of a different strain, so on IV-12 inoculation with the organism obtained from the case "Gold" was made. The results with autopsy are given below (case "Gold," Rabbit IV).

Rabbit V.—This animal was repeatedly inoculated with an emulsion from the growth on glycerin agar tubes of organisms from Case "Rand." The inoculations occurred on I-11, I-19, I-28, II-1, II-10, III-2, III-29, IV-7, IV-23, and IV-27.

From four days to a week after each one of the inoculations there were very definite tenderness and lameness in the larger joints. There is still marked lameness in the left fore leg three weeks after the last inoculation. The animal has not yet been killed.

Rabbit VI.—I–29: Inoculated intravenously with an emulsion made from the growth on six glycerin agar tubes (twenty-four hours' growth). The organism was obtained from the right shoulder of Rabbit III. There was no evident effect, and on II–4 a second similar inoculation was made. One week following this there were swelling and tenderness of the left shoulder. The animal was quite lame, would not put left fore foot to the ground. The right hind leg also seemed stiff and painful. On II–17 another inoculation similar to the first two was made. Three days later the swelling and lameness of the joints again became very marked. This lameness lasted for several days.

III–1: Another similar inoculation was made with similar results, and the rabbit died on III–7.

At autopsy it was found that the right shoulder contained an excess of sticky, slightly turbid fluid. The inner surface of the capsule was injected. There was no erosion of the cartilage. Similar slight changes were found in the left shoulder and both hips. The other joints all appeared normal on macroscopical examination. The internal organs showed no gross macroscopical lesions.

Cultures made from the left knee, left elbow, and left hip showed the growth of a moderate number of streptococci, corresponding in all characteristics to those inoculated. Cultures from the right knee were sterile. From the heart's blood, liver, and right kidney there was a very profuse growth of streptococci. Coverslips made from the heart's blood, liver, and kidney showed a moderate number of diplococci, while in those made from the left shoulder no cocci could be found after a prolonged search. Unfortunately, smears were not made from the other joints.

Sections were made from the head of the left femur, but practically no changes could be made out.

Finding that the results obtained by inoculation of this streptococcus agreed quite closely with those obtained by other observers with inoculation of the so-called "Micrococcus rheumaticus," it was decided to try streptococci from other sources in a similar manner. The following protocols give the results obtained with six other races of streptococci from various sources.

STREPTOCOCCUS NO. 2223.

This was obtained at autopsy from the peritoneal cavity of a man, aged fifty-seven, dying from an acute terminal infection complicating carcinoma of the stomach. There was no arthritis or endocarditis, and no history was obtained of rheumatism.

INOCULATION EXPERIMENTS.

Rabbit I.—Inoculated I–19–'04, intravenously. The emulsion was made from the growth on four glycerin agar tubes (twenty-four hours' growth). No lameness or swelling of the joints was made out before death, which occurred after forty-eight hours. At autopsy there were no macroscopical lesions in any joint. A pure culture of streptococcus was obtained from the heart's blood. No cultures were made from the joints. The organism obtained from the heart's blood in this case was repeatedly transferred on glycerin agar and then inoculated into another rabbit.

Rabbit II.—Inoculated IV-18-'04, intravenously. The emulsion was made from the growth on seven glycerin agar tubes (twenty-four hours' growth). The organism was obtained from Rabbit I.

On the third day after inoculation the rabbit was stiff and lame in both hind legs. There was considerable swelling of the left tarsal joint. This tenderness and swelling of the joints were more marked on the fourth day, when death occurred.

Autopsy.—The right knee, both hips, and both elbows appeared quite normal on gross examination. The tissues about both tarsal joints were very edematous, and the joints contained an excess of turbid fluid. Both shoulders also contained an excess of turbid fluid, the joint capsules being distended and reddened. The exudate was not so sticky as seen in some of the other cases. The cartilage appeared unaffected. The left knee was also distended with turbid fluid; no erosion of the cartilage. No gross lesions were made out in the internal organs, except in the heart. Both segments of the initial valve showed considerable thickening along the free margins. One of the segments was removed and sections made. These show a typical acute valvular endocarditis. There is marked thickening and infiltration with polymorphonuclear leucocytes and, in places, minute ulcers are seen.

Cultures were made from the heart's blood, spleen, liver, kidney, right tarsus, right and left shoulders, right knee. In all cultures there was a moderately profuse growth of streptococci. In smears made from the heart's blood no cocci were found. A few diplococci were present in smears made from the spleen and liver, and they were very numerous in the kidney smears. In coverslips made from the left knee very numerous dipplococci were found; no chains were seen. In the coverslips made from both shoulders and left ankle a great many diplococci were found, and these were sometimes collected into short chains of three to five pairs.

STREPTOCOCCUS NO. 2228.

This streptococcus was also obtained at autopsy from a case of puerperal septicemia with acute endocarditis and pericarditis. Death occurred three weeks after abortion, previous to which time the patient had been quite well. There was no arthritis. Streptococci were obtained from the heart's blood during life and the clinical features of the case were those of septicemia.

INOCULATION EXPERIMENTS.

Rabbit I.—Inoculated I-23-'04, intravenously, the emulsion being made from the growth on two glycerin agar tubes (forty-eight hours' growth). On the third day there were noted some lameness and stiffness in the right hind leg. This continued for two days. On I-29-'04 the animal was reinoculated with the emulsion from four glycerin agar tubes, and again on II-4-'04 with the emulsion made from six tubes (twenty-four hours' growth). Three to four days after each inoculation the tenderness and lameness became more marked. With the last inoculation the lameness was most marked in the left fore leg.

On II-9-'04 the rabbit was killed. At autopsy the tissues about the left shoulder were found to be very edematous and swollen. The joint was much distended, and the capsule was filled with a purulent fluid containing flaky masses. The right knee joint was also found to be affected. On opening the capsule of the joint a sticky, purulent fluid exuded. The capsule was found reddened, especially along its junction with the cartilage. The right shoulder also showed a mild inflammatory reaction. The right elbow was hardened *in toto* without opening. The other joints all appeared normal. The internal organs showed no gross lesions.

Cultures made from the heart's blood, liver, spleen, kidney, right elbow, left knee, right knee, and right shoulder showed no growth whatever. On the plates made from the left shoulder there occurred quite a profuse growth of streptococci, resembling those inoculated. Three loops of the fluid were inoculated in each plate, and on each about fifty colonies developed. Coverslips made from the exudate in the left shoulder showed a moderate number of diplococci; no chains could be found. It was impossible to find any diplococci or other bacteria in coverslips made from any of the other joints. Sections were made from the right shoulder, left shoulder, right knee, and right elbow. The left shoulder showed the most marked changes. There is an abundant purulent exudate, the cellular elements of which are mainly polymorphonuclear cells, but scattered among which are seen many larger mononuclear cells. The tissues about the joint also show a marked polymorphonuclear infiltration, and there are everywhere very marked edema and congestion of the blood vessels. Notwithstanding the marked inflammatory reaction, however, the free surface of the cartilage is perfectly smooth. The right shoulder shows a milder infection, though there is a considerable inflammatory exudate, containing many polymorphonuclear leucocytes, with thickening and infiltration of the capsule, especially of the villus projections about the edges of the joint. The right elbow also shows quite a marked inflammatory reaction of the same nature as seen in the shoulders. As this joint was not opened before hardening, the increased exudate into the joint is very well shown. The tissues outside the joint do not show such marked changes as were seen in the left shoulder. The right knee shows the slightest changes of all, though even here the congestion and infiltration of the villi is very well marked.

Rabbit II.—Inoculated with emulsion made from growth on four glycerin agar tubes of organism obtained from the joint of Rabbit I. Death occurred in twelve hours. Joints normal.

Rabbit III.—Inoculated III-2-'04, intravenously. The emulsion was made from growth on three glycerin agar tubes of organisms obtained from joint of Rabbit I. Two days later the rabbit was very lame in the left fore leg, and it seemed sick and not inclined to move about. This lameness and apparent weakness and sickness continued until III-7-'04, when the animal began making inco-ordinated movements, throwing itself about in the cage and, when placed on the floor, running about violently in various directions, apparently not seeing where it was going and running its head into the walls. Respiratory movements were very jerky and rapid. The animal died in the afternoon.

Autopsy.—Joints: The muscles and tissues about the left shoulder joint appeared very edematous. On opening the joint the capsule was found to be distended with a moderate amount of a yellowish, purulent, cloudy fluid. The cartilage appeared normal. The inner surface of the capsule was injected. The right shoulder joint resembled the left. The capsules of the left knee and of both hips were also slightly injected, and in these joints there was a slight increase in the amount of fluid which was slightly cloudy. The other joints appeared normal.

Heart: There was quite marked dilatation, especially of the right side. The tricuspid and pulmonary valves appeared normal. The aortic valves also appeared thin and normal. Adhering to the edge of one of the cups of the mitral valve was a long clot which, on attempting to remove it, was found to be a thrombus attached to a rough area on the valve. This area was covered by small vegetations.

The liver was congested. The spleen appeared normal. The left kidney was larger than the right and contained numerous small abscesses the size of a pinhead. The pelvis of the left kidney was injected and distended, and contained a purulent fluid. The urine was very cloudy, and contained a large amount of sediment. The bladder mucosa was injected.

Cultures made from both shoulders showed numerous streptococci· There was also a growth of a few streptococci from the right hip. No growth, however, occurred in the cultures from the left knee and right elbow. Also there was no growth in the cultures made from the heart's blood. Streptococci also grew in the cultures from the liver, spleen, and right kidney. Cultures made from the urinary bladder and left kidney showed a pure growth of B. coli communis. It therefore seems probable that the abscesses in the left kidney and the urinary infection were due to a secondary infection, possibly local in origin.

Coverslips made from the exudate in both shoulders show a moderate number of diplococci. No chains were found. No bacteria could be demonstrated in smears made from either hip. Smears from the right kidney showed a moderate number of diplococci, while in smears from the urine only short rods could be discovered. No bacteria could be demonstrated in coverslips from the heart's blood or liver. The left shoulder joint was removed entire and decalcified, and sections were made. The joint contained a moderately purulent exudate, and there was a moderate grade of infiltration of the capsule with polymorphonuclear cells. The cartilage appeared normal. Sections through the left kidney showed numerous very small abscesses.

(This case illustrates well the occurrence of an endocarditis with involuntary, inco-ordinated movements, which by a stretch of the imagination might be called choreiform.)

Rabbit IV.—This rabbit was inoculated intravenously on IV–8–'04 with an emulsion made from the growth on four glycerin agar tubes of the streptococcus obtained from the joint of Rabbit III. Three days later the animal was very lame in the right hind leg. The stiffness extended to the other joints, but the right knee remained most affected and was considerably swollen. On IV-15-'04 the rabbit was killed, and an autopsy was performed immediately. On opening the right knee joint it was found to contain an excess of slightly turbid, sticky, mucoid, fluid, containing some small grayish flakes. The cartilage was smooth, but the lining of the capsule was hyperæmic. The left elbow also contained an excess of a similar fluid, and the capsule presented the same appearance. The right shoulder joint appearing distended with fluid, only a small puncture was made in order to obtain a culture, and the whole joint was then hardened unopened. The other joints appeared normal. There were no signs of endocarditis, and the other organs appeared normal, except the kidneys. These were pale, and showed on section quite numerous small pin-point areas which were grayish and resembled minute abscesses. Sections made from these kidneys show quite numerous small focal areas of infiltration with small round cells. The capsule is much thickened, and there is a new growth of connective tissue entending some distance below the surface. Practically no polymorphonuclear infiltration is seen anywhere.

Cultures were made from the internal organs and joints. No growth occurred in cultures from the heart's blood, spleen, liver, or kidney. The cultures from the left shoulder, left knee, and right elbow were also sterile, while in the cultures from the right knee, right shoulder, and left elbow there developed a considerable number of streptococcus colonies.

STREPTOCOCCUS OBTAINED FROM CASE "M'CABE."

This was a case of cardiac hypertrophy and dilatation in a man aged thirty-one. He had been a stoker and worked very hard. No other etiological factor could be obtained. He had never had rheumatism, any form of arthritis, or any acute infection. The patient was admitted to the hospital on I-25, and from this time until III-5 he suffered with severe symptoms of cardiac insufficiency, but there was no fever. On II-5, however, the temperature suddenly rose, and he began having high fever, sweating, and delirium. Blood cultures on III-7 showed the presence of streptococci in large numbers, 140 colonies to 1 c.c. of blood. The patient died on III-8. At autopsy marked sclerosis of the coronary vessels was found with fibrous myocarditis, but there was no acute or chronic endocarditis. In addition, there were infarction of the lungs and acute pleurisy.

INOCULATION EXPERIMENTS WITH ORGANISM OBTAINED FROM BLOOD DURING LIFE.

Rabbit I.—Inoculated III-29-'04, intravenously, with emulsion made from twenty-four-hour growth on six glycerin agar tubes. On the following day the rabbit was found to be quite lame in the right fore leg. This lameness increased, and the tenderness gradually spread to the other joints. The animal could not be induced to move about, and passive movements of the joints seemed to cause pain. No evident swelling in any of the joints could be made out. Three days after inoculation the animal began to show general convulsive twitchings of all the extremities. These convulsive movements increased up to the time of death, which occurred on the following day.

Autopsy.—The pericardium contained a moderate increase of slightly turbid, bloody fluid. The endocardium was slightly blood-stained; no endocarditis made out. No abscesses were found in the liver, spleen, kidneys, or lungs. The tissues about the right knee were slightly edematous. The lining of the capsule was reddened and covered with a thick, sticky, turbid fluid. The capsule of the joint was moderately distended. There was also some edema about the left knee. The entire joint was hardened unopened. Both elbows and the left knee showed changes similar to those seen in the right knee. The involvement of the right tarsus was greater than that of the other joints, the edema of the tissues about being very marked and the exudate quite purulent. No changes could be detected in the right hip, and in the left hip there was merely slight reddening of the lining of the joint, and a moderate increase of sticky, slightly turbid fluid.

Sections were made from the elbows, knees, shoulders, and tarsal joints, the left knee and right elbow being hardened unopened. In all the joints examined there was found a mucopurulent exudate, with a slight infiltration of the capsule and synovial membrane with polymorphonuclear leucocytes, the most marked changes being noted near the folding of the membrane upon itself about the bone, while the cartilage in all cases was quite smooth and appeared normal.

Coverslips made from the pericardium showed quite numerous diplococci and short chains of two or three pairs of cocci. In those made from the heart's blood, liver, and kidneys diplococci were found in considerable numbers, and also a few short chains consisting of three or four pairs of diplococci; but no long chains were found. In coverslips made from both elbows, both tarsal joints, right shoulder, right knee, and left hip, cocci were found, though in variable number, very many being present in the joints most involved, while in those less involved fewer were present. In all cases the cocci were in the form of diplococci, occasionally short chains of two or three pairs being seen. In all cases there were numerous polymorphonuclear cells, though small mononuclear cells were also present in considerable numbers. The cocci were in all cases extra-cellular.

Cultures from the heart's blood, kidney, and liver, showed typical streptococci growing in broth into long chains. There occurred also a moderately profuse growth on plates made from the left tarsal joints, left hip, right knee, and right shoulder. In all cases the growth was a pure one of typical streptococci growing into long chains.

STREPTOCOCCUS FROM CASE "GOLD."

This case was one of empyema, probably following an acute lobar pneumonia, though the onset was rather insidious. There had never been any rheumatism or arthritis. The heart sounds were clear. On aspiration of the chest turbid, purulent fluid was obtained, cultures from which gave a pure growth of streptococci. The chest was later freely opened, drainage established, and the patient made a complete recovery.

INOCULATION EXPERIMENTS.

Rabbit I.—This rabbit died twenty-four hours after inoculation intravenously with an emulsion made from the twenty-four-hour growth on five glycerin agar tubes. At autopsy no joint involvement could be made out, though coverslips from the right knee showed a few puss cells, and a considerable number of diplococci and short chains of cocci. Cultures and coverslips from the internal organs all showed streptococci.

Rabbit II.—This rabbit died twelve hours after inoculation with an emulsion made from the twenty-four-hour growth on three glycerin agar tubes. No changes in any joints were found at autopsy. Cultures showed a general septicemia, but cultures from the joints were negative.

Rabbit III.—Inoculated IV–23–'04 with an emulsion made from the twenty-four-hour growth on two glycerin agar tubes. The animal did not appear very sick following this injection, until the fourth day when the lameness was quite marked. Both fore legs and the right hind leg seemed affected. The animal moved about with difficulty. This condition of stiffness and lameness persisted and increased until IV–30–'04, seven days after inoculation, when death occurred.

Autopsy showed no endocarditis and no purulent foci in any of the internal organs. Both knees appeared normal. There was considerable edema about both tarsal joints, and the capsules were reddened and distended with sticky, turbid fluid. The right hip showed a slight turbid exudate and reddening of the capsule. The left elbow and both shoulders also showed a similar mild involvement. The left hip and right elbow appeared normal. Both shoulder joints were hardened entire. Sections through these showed the joint moderately distended with a muco-purulent exudate and an infiltration of the capsule. In the left shoulder the cartilage was somewhat roughened and irregular, but whether this was due to the inflammation or to manipulation could not be determined.

Coverslips from the kidney and spleen showed a moderate number of diplococci. In the heart's blood no cocci could be definitely detected. In coverslips from the right hip, the right ankle, and the left knee diplococci were present in considerable numbers; no chains could be found. In the left ankle the diplococci were in much smaller numbers, and a few short chains of two and three pairs were found.

Cultures made from the spleen and kidney showed a moderately profuse growth of streptococci. The cultures from the liver and heart's blood showed a very scant growth of streptococci. They were present in cultures from the left knee, right tarsus, and right shoulder in moderate numbers; much fewer in the left ankle, while in cultures made from the right knee, right elbow, and left shoulder no growth occurred.

Rabbit IV.—This is the same rabbit as Rabbit IV under those inoculated with organism "Rand." After repeated inoculation with this organism and repeated attacks of lameness, it was thought that a moderate grade of immunity had been established, so that it was inoculated with the organism obtained from the case "Gold" which appeared more virulent. Inoculated IV-12-'04 with emulsion made from growth on two glycerin agar tubes. After three days the animal did not appear lame or sick. It was again inoculated with an emulsion made from the growth on four glycerin agar tubes. Four days later the rabbit died. During life no swelling of the joints was detected; the animal did not appear lame.

Autopsy.—No purulent foci in the heart, lungs, liver, spleen, or kidneys. The right testicle was found to be swollen, the capsule red and hemorrhagic. No area of softening or abscess formation could be made out on section. Joints: The right knee was larger than the left. The joint contained an excess of thick, sticky, turbid fluid, while the capsule was reddened and showed minute areas of injection, but the cartilage appeared normal. The left knee had a similar appearance, though was not so swollen as the right. No changes were made out in either hip. The elbows, left shoulder, and left tarsus also appeared normal. The right shoulder and right ankle showed changes similar to those seen in the knees.

Coverslips made from the heart's blood, liver, spleen, and kidney all showed diplococci. A few very short chains of two or three pairs were also seen. In coverslips from both knees and from the right shoulder numerous diplococci were found. In coverslips from the left shoulder the diplococci, while present, were very few in number. In cultures made from the heart's blood, liver, kidney, spleen, and testicle there occurred a pure growth of streptococci. There occurred also a pure growth in the cultures from the knees and from the right shoulder; in these, however, the number of colonies was much less than in cultures from the internal organ.

Sections were made from the right knee and right shoulder. These show, in addition to the acute changes seen in the other rabbits, very marked thickening of the villous outgrowths and an infiltration of them with polymorphonuclear leucocytes. There is marked endarteritis of the vessels of these villi. The capsule is thickened, and in places the cartilage covering the end of the bone is much eroded and has become fibrous and infiltrated. The right testicle shows a diffuse acute inflammation and foci where the polymorphonuclear infiltration is more marked, but without true abscess formation.

STREPTOCOCCUS OBTAINED FROM CASE "D."

This was a case of acute, apparently uncomplicated appendicitis. Appendectomy was performed, following which the patient continued to have high fever, sweating, and the clinical features of septicemia. There were no signs of peritonitis; there was no arthritis. Blood cultures showed the presence of streptococcus. The patient died. Permission for autopsy could not be obtained.

INOCULATION EXPERIMENTS WITH STREPTOCOCCUS OBTAINED FROM BLOOD.

Rabbit I.—Innoculated IV-6-'04 with emulsion made from the twenty-four-hour growth on six glycerin agar tubes. Three days later the animal became lame in the left fore leg, and it also showed some general stiffness of all extremities. There was gradual improvement of this condition, and on IV-12-'04 a second inoculation was made of the growth on three glycerin agar tubes. As following this the animal continued to show no symptoms, a third inoculation of the growth on four glycerin agar tubes was made on IV-15-'04, and a fourth one of the growth on six glycerin agar tubes on IV-16-'04. Two days later the rabbit appeared very lame on the left hind leg. The lameness increased, the swelling of the left tarsus became more marked, and on IV-21-'04 the rabbit was killed.

Autopsy.—No focal lesions could be made out in any of the viscera. All the joints appeared normal, except the left shoulder and the left tarsus. These joints showed exudate and capsular inflammation, exactly as seen in the other rabbits.

Coverslips made from heart's blood, spleen, liver, and kidney were negative. Neither were any cocci found in the coverslips made from the right shoulder and right knee. In those made from the left shoulder, however, a very few diplococci were found. Cultures made from the heart's blood, liver, spleen, and kidney, and from both knees, were also negative, but in the cultures from the left shoulder a moderate growth of streptococci occurred.

STREPTOCOCCUS OBTAINED FROM CASE "L."

This was a child aged three years, suffering with tuberculosis of the tibia. The knee joint was not involved. Operation was performed, and the child was doing well when it developed scarlet fever, contracted apparently from another child in the ward. Following the acute symptoms of the scarlet fever there developed an acute cervical adenitis. The glands were incised, and from the purulent contents cultures were made which showed a pure growth of streptococci.

INOCULATION EXPERIMENTS.

Rabbit I.—On IV-28-'04 this rabbit was inoculated intravenously with an emulsion made from the twenty-four-hour growth on three glycerin agar tubes. Death occurred twenty hours after inoculation. No distinct changes could be made out in any of the joints. Cultures made from the various organs showed streptococci, and they also grew in cultures made from both knee joints.

Rabbit II.—This rabbit was inoculated V-4-'04 with an emulsion made from the twenty four-hour growth on one glycerin agar tube. No lameness that could be detected resulted, and death occurred after forty-eight hours. No gross lesions could be detected in this rabbit. Both knees appeared a little injected, but the changes were not definite.

Coverslips showed diplococci, and short chains in the internal organs and also in both knees. Streptococci were also cultivated from both knees as well as from the internal organs.

Rabbit III.— On V–16–'04 this rabbit was inoculated with one-fourth of an emulsion made from the growth on one glycerin agar tube. After two days there was quite evident lameness in the left hind leg. This lameness continued, there appeared general stiffness, and on V–21–'04, or five days after inoculation, death occurred. No macroscopic focal lesions were found in any of the internal viscera. The joints were all carefully examined, and no changes could be made out in any of them except the right tarsus, both hips, and both shoulders. These showed a moderate distension with turbid fluid, injection of the capsule, etc., exactly as was seen in the other rabbits, This was also well shown in the microscopical examination of the sections made through the left shoulder. Coverslips made from the heart's blood of this rabbit showed quite long chains of cocci, some of them composed of twenty to thirty cocci. (This was the only case in which this was noted.) Coverslips from the affected joints, however, showed only diplococci. Cultures made from the heart's blood, liver, and kidney showed quite a profuse growth of streptococci. Streptococci in smaller numbers also grew from the right shoulder, right knee, and left hip. No growth occurred in the cultures from the left knee. In the cultures made from this case, in addition to the streptococci, there also grew from the heart's blood, liver, kidney, and right shoulder a few large colonies, which were identified as B. coli. As they occurred in such small number in only a part of the cultures, and the autopsy was not performed for some hours after death, it is probable that this was a postmortem invasion or a contamination.

It will thus be seen that experiments were undertaken with six races of streptococci aside from those with the race obtained from a possible rheumatic endocarditis Case "Rand." The sources of these various races were: peritonitis following carcinoma of the stomach; puerperal fever-autopsy; blood during life in terminal septicemia following myocarditis; empyema; blood during life in septicemia following appendicitis; scarlet fever adenitis.

The diversity in the sources of these races renders it impossible that they could all have had any association with rheumatism, so that we could not have been working always with the so-called "Micrococcus rheumaticus."

Our experience, as shown by the protocols, shows no essential difference in the results obtained between the several races studied, except in the virulence; that is, the amount necessary to produce the desired results. So, too, a careful comparison of our results with those obtained by Poynton and Paine, and others, fails to show any essential differences. The essential point claimed for the characterization of the specific coccus causing rheumatism is its ability to produce arthritis and endocarditis when inoculated intravenously into rabbits.

With all seven races studied intravenous inoculation of amounts insufficient to cause death of the animals within six or seven days led to the production of mild grades of arthritis. The only reason we have to offer why this arthritis has not previously been noted by all observers who have done experimental work with streptococci is that usually such work is done with the idea of testing the pathogenicity of organisms, usually determined by the amount and time necessary to produce a fatal result, and when post-mortem examinations were made the joints have not been carefully studied as a routine procedure. During life a rabbit having arthritis will usually remain quiet in one corner of the cage, and it is only when the rabbit is placed on the open floor and urged to move about that the lameness is detected. So, too, in most cases the swelling of the joint, unless extreme, is rather difficult to detect through the thick skin and fur. Often a considerable distension of the joint and edema of the surrounding tissues has been found after dissecting away the skin, when previously it could not with certainty be detected. In many cases the joint affection is mild, and unless one were especially interested in looking for it, it might be overlooked. It is only by making a routine examination of all joints that the lesions are discovered.

From the work given it seems that, when streptococci from whatever source are inoculated intravenously into a rabbit, they tend early to localize in the joints, even before any definite lesions can be detected. In Rabbit I, Group Case "Gold," twenty-four hours after inoculation; Rabbit I, Group Case "L," twenty hours after inoculation; and in Rabbit II, Group Case "L," forty-eight hours after inoculation, streptococci could be found in the joints with no evidence of inflammation. In another rabbit inoculated with streptococci from a case of meningitis, death occurred thirty-six hours after inoculation, and in both knees, which macroscopically appeared normal, streptococci were found on cover-slips and cultures. On the other hand, in one rabbit—Rabbit II, Group Case "Gold"—dying twelve hours after inoculation, no organisms could be grown from the joints. It is therefore probable that after intravenous inoculation with streptococci these organisms very soon are found in the joints, and finding here a *locus minoris resistentiae*, or conditions favorable for their growth, may persist here and set up a mild grade of infection. In certain cases the organisms may disappear from all the other parts of the body, and remain in the joints, as in Rabbit IV, "Streptococcus No. 2228," where one week after infection no organisms could be cultivated from any of the internal organs, while they readily grew from certain joints.

In most cases the joint affection set up is mild and tends to recovery. This tendency to recover is well seen in Rabbit IV, Group "Rand," in which for four months arthritis was repeatedly induced, and just as often recovery took place.

In most cases the pathological changes in the joints are mild, consisting mainly of edema about the joint, moderate increase of fluid within the joint, the fluid becoming turbid, sticky, and tenacious; injection of the capsule and slight infiltration, mainly of the villi, with polymorphonuclear leucocytes. In only one or two joints did the appearance resemble that seen in severe septic arthritis. It must be said that the features were more like those seen in acute articular rheumatism, though in the cases which I have seen of articular rheumatism with exudate into the joints the exudate has always been quite thin and fluid, though frequently clotting quickly after removal.

Endocarditis.—In two of the rabbits a true endocarditis was present. One of them was inoculated with streptococcus from the peritonitis case, the other from the puerperal fever case. Section through the valves in both of these cases showed a typical acute valvular endocarditis. In several of the other rabbits there was slight thickening of the valves noted, which at first was thought possibly due to endocarditis, but on section they were found to be merely slight thickenings, too old to have been due to the inoculations. In both of the cases the mitral valve was the one affected, and the involvement consisted of small vegetations along the edge of closure. While in this series of inoculation experiments endocarditis did not occur so frequently as in some of the series reported by English observers, yet the fact that typical endocarditis occurred with two of the organisms studied, and that this endocarditis was indentical with that described by the other observers, makes a differentiation of the organism on this ground untenable.

Chorea.—Several observers have claimed to have produced chorea in rabbits by the intravenous injection of the "Micrococcus rheumaticus." I have not been able to find any complete description by Poynton and Paine of the symptoms resembling chorea produced by them, though they repeatedly refer to having produced chorea in rabbits. Beattie describes one rabbit in which on the second day after inoculation "there was very definite chorea, with twitching of the head and eyes to the right side. When the animal attempted to walk it fell to the right side and the twitching became much more marked." Two days later "the chorea was much less marked," and on the following day "the twitchings had practically ceased."

Referring to the protocols previously given, it will be seen that Rabbit I, Group "McCabe," and Rabbit III, Group No. 2228, showed similar convulsive inco-ordinate movements before death. Most clinicians, however, would doubt the diagnosis in a case of chorea lasting two or three days, and I should hardly like to say that the features in *my* rabbits at least resembled even remotely a case of chorea. In Beattie's case, from the description of movements, always in one direction, one would think it more probable that a focal abscess or a localized meningitis had been present.

It may be stated that, while slight morphological and cultural differences existed between the various races of streptococci studied, none of these were constant enough to speak of a distinct variety. Each one differed slightly from the other in its manner of growth in bouillon, its growth in milk, etc. To make such comparative studies of any value, they should be repeated at intervals over a considerable length of time, to make certain that the characteristics have at least a fair degree of constancy. This has not yet been done with the organisms studied. So far as length of chain is concerned, corresponding with the observations of many others, we could determine no constant character, as this property seemed to depend much more on the character and reaction of the medium used than on the race of the organism. It is worth while, however, referring again to the fact that in smears made from the joints, and also to a considerable degree from the organs of rabbits inoculated with streptococci, long chains are almost never met with, the cocci appearing as diplococci or as very short chains composed of a few diplococci, and in these pairs the individual cocci are usually somewhat flattened on one side, the flat sides approximated, causing the cocci to have a long diameter transverse to the length of the chain. It may be that this fact is responsible for the so-called organism of rheumatism having sometimes been called a diplococcus and again a streptococcus by various observers.

It will be seen from the protocols that there was considerable variation in the pathogenicity as measured by the lethal dose of the races studied. Thus, while with certain of the organisms an emulsion made from the growth on six to eight tubes could be safely inoculated, in the case of the streptococcus obtained from the cervical adenitis in scarlet fever, one-fourth of a tube caused death in five days when so inoculated. It is of interest that this race from a local lesion should have been so much more pathogenic than those obtained from general infections.

CONCLUSIONS.

Arthritis and endocarditis may be produced by the intravenous inoculation of rabbits with streptococci from various sources, and the results obtained are quite similar to those described as resulting from the inoculation of the so-called "Micrococcus" or "Diplococcus rheumaticus."

Therefore the description of a distinct variety or species of streptococci based on this property of causing endocarditis and arthritis is unwarranted. Whether the evidence is sufficient that acute rheumatic fever is simply a form of streptococcus septicemia it is not intended to discuss in this paper.

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